2025 | Vol 6 | Issue 47

Ophthal Focus

Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you 'Ophthal Focus' which contains latest and interesting news in the field of Ophthalmology.

This issue contains

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- **Association between obesity and orbital fat expansion in proptosis of thyroid eye disease**
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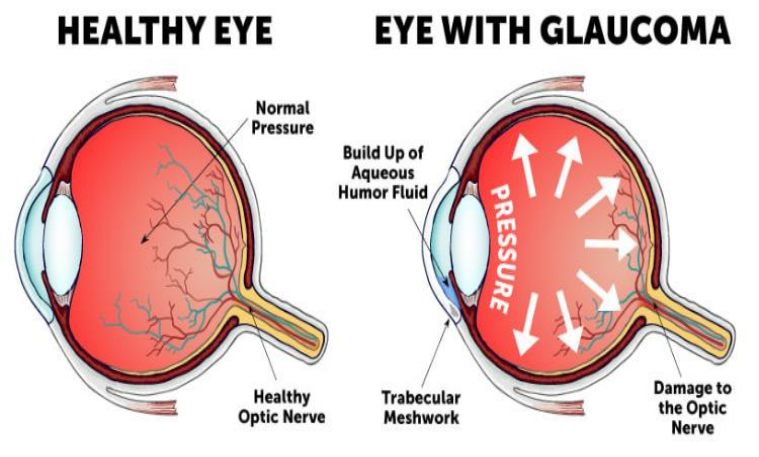
Medical Team, Micro Labs Limited

Comparison of rates of change in Ganglion Cell- Inner Plexiform Layer and Retinal Nerve Fiber Layer thickness using Optical Coherence Tomography

INTRODUCTION



GLAUCOMA

Glaucoma is a progressive optic neuropathy characterized by visual field (VF) loss resulting from the degeneration of retinal ganglion cells and their axons. Since glaucomatous damage is irreversible, early detection of disease progression is vital for effective management. Assessing glaucoma progression involves both structural and functional diagnostic methods. The VF test is a commonly used functional diagnostic tool, while structural evaluations include clinical optic disc examination and optical coherence tomography (OCT). The Cirrus HD-OCT platform's guided progression analysis (GPA) software is designed to track structural changes in glaucoma by analyzing the retinal nerve fiber layer (RNFL) and the macular ganglion cell-inner plexiform layer (GCIPL). Pseudo-exfoliation glaucoma (PXG) is linked to elevated intraocular pressure (IOP) and greater IOP fluctuations compared to primary open-angle glaucoma (POAG).[1] Lee WJ et al. analyzed the rates of GCIPL and RNFL thinning among control subjects, POAG patients, and PXG patients using the GPA program. Their findings revealed that GCIPL thinning occurred at a faster rate in PXG patients compared to those with POAG and the control group.[2] This study aimed to evaluate and compare the rates of change in GCIPL and RNFL thickness among control eyes, POAG eyes, and PXG eyes using the GPA program of OCT.

Patients with PXG had the highest rates of RNFL thinning and GCIPL. The study found that the rate of RNFL and GCIPL thinning was unaffected by the stage of glaucoma.

METHODS

Data from 60 patients with POAG, 60 with PXG, and 30 control patients were analyzed retrospectively. Glaucoma patients were categorized into mild (MD > −6.00) and moderate-to-

severe (MD < −6.00) stages. The average, superior, and inferior quadrant thinning rates of the GCIPL and RNFL, measured in micrometers per year using the OCT-GPA program, were compared across the groups. Inclusion criteria required a best-corrected visual acuity of 20/40 or better in the study eye, spherical refraction within ±5.0 diopters, cylinder correction within ±3.0 diopters, open angles on gonioscopy, at least three years of follow-up, and a minimum of six consecutive OCT measurements.

RESULTS

The central corneal thickness (CCT) was significantly greater in the control group compared to both POAG and PXG patients (p=0.018, p=0.041). PXG patients exhibited significantly higher average GCIPL thinning rates than the control group and POAG patients (p<0.001). Similarly, average RNFL thinning rates were significantly greater in PXG patients than in the control and POAG groups (p=0.001 and p=0.028, respectively). In comparing mild POAG patients with the control group, no significant difference was observed in inferior RNFL thinning rates (p=0.158), while all other measurements showed a higher thinning rate in POAG patients. Among POAG patients, significant correlations were found between average GCIPL thinning rates and average RNFL thinning rates (p=0.041), as well as between superior GCIPL thinning rates and both superior and inferior RNFL thinning rates (p=0.004, p=0.045). In PXG patients, GCIPL and RNFL thinning rates were correlated across all quadrants (Table 1).

Table 1. Association Between the RNFL and GCIPL Rates of Change in the Control Group, POAG, and PXG Eyes

	Control (n=30)			POAG (n=60)			PXG (n=60)		
RNFL	**Average**	**Superior**	**Inferior**	**Average**	**Superior**	**Inferior**	**Average**	**Superior**	**Inferior**
GCIPL									
Average	0.177	0.243	0.179	0.265	0.123	0.153	0.530	0.496	0.516
	p=0.348	p=0.195	p=0.344	**p=0.041**	p=0.350	p=0.242	**p<0.001**	**p<0.001**	**p<0.001**
Superior	0.200	0.240	0.0002	0.345	0.368	0.260	0.477	0.443	0.452
	p=0.290	p=0.201	p=0.999	**p=0.007**	**p=0.004**	**p=0.045**	**p<0.001**	**p<0.001**	**p<0.001**
Inferior	0.124	0.108	0.235	0.002	−0.190	−0.067	0.461	0.410	0.455
	p=0.515	p=0.571	p=0.211	p=0.989	p=0.146	p=0.613	**p<0.001**	**p=0.001**	**p<0.001**

RNFL- Retinal nerve fibre layer, GCIPL- Ganglion cell – Inner plexiform layer, POAG- Primary open angle glaucoma, PXG- Pseudo exfoliation glaucoma. Correlation coefficients (rho) and p values are shown. Pearson correlation was used for evaluating correlation. A p value<0.05 is considered as significant.

DISCUSSION

Several studies have investigated the rates of GCIPL and RNFL thinning in both healthy individuals and glaucoma patients. Belghith et al. documented a GCIPL thinning rate of −0.11 µm/year in healthy subjects and −0.18 µm/year in POAG patients using the Spectralis OCT.[3] In the current study, GCIPL thinning rates measured with Cirrus OCT software was −0.23 µm/year in normal eyes, −0.64 µm/year in POAG eyes, and −1.06 µm/year in PXG eyes. Similarly, RNFL

thinning rates were observed at −0.33 µm/year in normal eyes, −0.86 µm/year in POAG eyes, and −1.33 µm/year in PXG eyes. Lee et al. previously reported GCIPL thinning at −1.46 µm/year and RNFL thinning at −1.31 µm/year in PXG patients.[2]

CONCLUSION

The rates of GCIPL and RNFL thinning are significantly faster in PXG eyes compared to POAG eyes and the control group. POAG patients also exhibited higher GCIPL and RNFL thinning rates than the control group. In both glaucoma types, there was no significant difference in GCIPL and RNFL thinning rates between the mild and moderate-to-severe stages. A positive correlation was observed between GCIPL and RNFL thinning rates as glaucomatous damage progressed. These findings highlight the more aggressive nature of PXG compared to POAG.

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Association between obesity and orbital fat expansion in proptosis of thyroid eye disease

INTRODUCTION

In thyroid eye disease, obesity has been associated to increased orbital fat and, as a result, more severe proptosis.

Thyroid eye disease (TED) is an autoimmune inflammatory condition that impacts the orbital and periorbital tissues, leading to unilateral or bilateral proptosis. The expansion of the periorbital tissues can cause diplopia, and if the disease progresses to dysthyroid optic neuropathy, it may threaten vision. The growth of orbital fat is a key pathological factor in the periorbital enlargement seen in TED.[1] The potential association between obesity and orbital fat accumulation in thyroid-associated orbitopathy has yet to be established. Lacheta et al. highlighted the ability of orbital fibroblasts to transform into adipocytes.[2] Khong et al. also observed increased adipogenesis in thyroid ophthalmopathy, which involved the proliferation and differentiation of adipocytes.[3] This study aimed to examine the relationship between obesity and proptosis in TED and assessed whether individuals who underwent orbital fat decompression surgery had a higher average body mass index (BMI). Additionally, the study investigated the connection between obesity and the

severity of proptosis, as well as the correlation between obesity and the volume of fat removed during orbital fat decompression surgery.

METHODS

This observational study retrospectively included 87 participants who underwent orbital fat decompression surgery for thyroid eye disease. The primary outcome measures were the average BMI, and the percentage of participants classified as overweight or obese, compared to the general Taiwanese population. Secondary outcome measures focused on the relationship between obesity and proptosis severity, the volume of fat removed, and thyroid status.

RESULTS

The average BMI of the study sample (25.59±4.36 kg/m²) was significantly higher than that of the general Taiwanese population (24.5 kg/m²; P=0.012). Participants who were overweight (19.52±3.52 mm) or obese (21.25±3.76 mm) showed significantly more severe proptosis than those without overweight (18.05±3.37 mm) and without obesity (18.09±3.02 mm; P=0.029 and P<0.001, respectively). Additionally, a significantly greater volume of orbital fat was removed in the obese group (4.61±1.17 ml) compared to the non-obese group (3.57±1.12 ml; P=0.021). A positive correlation was found between BMI and the volume of fat removed (correlation coefficient = 0.291, P=0.005) (Figure 1). BMI was an independent factor predicting both proptosis severity (P<0.001) and the volume of orbital fat removed (P=0.02).

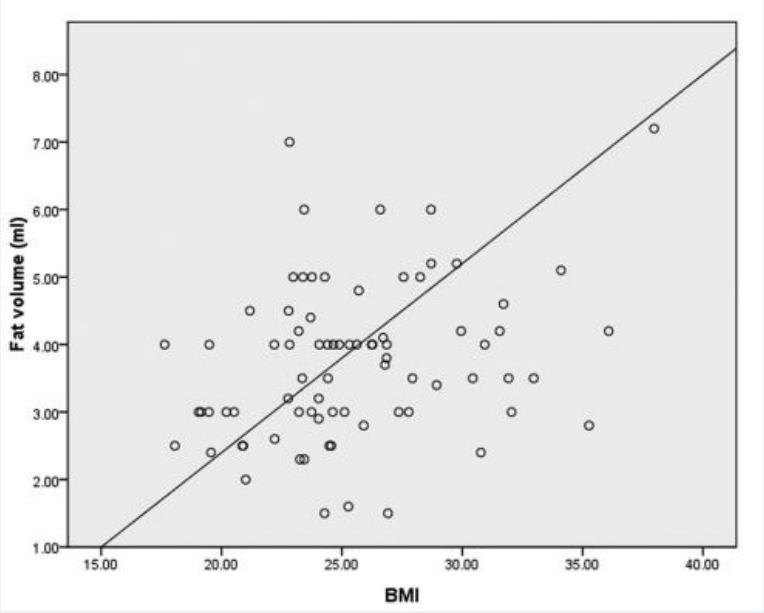

Figure 1. Relationship between orbital fat decompression operation removed orbital fat volume and BMI. Correlation coefficient=0.291, P=0.005

DISCUSSION

Participants who underwent orbital fat decompression surgery had a significantly higher average BMI compared to the general population. The study also found a higher prevalence of overweight and obesity in the study sample. Adipogenesis is the process in which pre-adipocytes develop into adipocytes, leading to fat expansion. When the body's metabolic balance is disrupted, excess fat

accumulation contributes to the development of obesity.[4] Lu et al. also demonstrated a relationship between obesity-related factors, such as BMI, and Graves orbitopathy.[5]

CONCLUSION

This study found an association between obesity, orbital fat expansion, and proptosis in TED. It showed that since orbital fat accumulation in thyroid-associated orbitopathy is related to obesity, weight management could play an important role in preventing severe exophthalmos in patients with thyroid orbitopathy.

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Determination of longitudinal changes in optic disc morphology and their association with peripapillary retinal nerve fiber layer thickness

INTRODUCTION

Even in cases of modest myopia, optic disc alterations happen early in childhood. Variations in RFL thickness across quadrants are associated with increasing myopia and aging and myopia therapy might have an impact.

Axial myopia, resulting from excessive growth of axial length (AL) during childhood, has become an epidemic in East Asia since the early 1990s and is expected to impact 49.8% of the global population by 2050.[1] As myopia increases, structural changes such as optic disc tilt (ODT) and peripapillary atrophy (PPA) are observed. Various studies using optical coherence tomography (OCT) imaging of the optic nerve head have indicated that the peripapillary retinal nerve fiber layer (RNFL) is thinner in myopic eyes compared to emmetropic and hyperopic eyes. However, the impact of ocular magnification on RNFL measurements in children is largely underexplored.[2] In the Anyang Childhood Eye Study (ACES) of 12-year-old children, Zhu et al. found a negative correlation between RNFL thickness (in the superior, inferior, and nasal quadrants) and increased AL in boys.[3] This study examined the long-

term relationships between myopic optic disc characteristics and OCT measurements of peripapillary RNFL thickness in young children with myopia.

METHODS

A prospective cohort study was carried out at a single site, involving children aged 7 to 16 years who took part in the PROM-Kids (Prospective Review of Myopia in Children) clinical cohort study from 2019 to 2022. The participants underwent annual evaluations, including cycloplegic refraction, axial length measurements, fundus photography, and OCT imaging, with corrections for ocular magnification. Children were categorized into low (LM, 0 to −3D), moderate (MM, −3.01 to −6D), and high (HM, >−6D) myopia groups, with or without treatment.

RESULTS

Data from 1,000 children (right eye) were analyzed, including 521 with a 2-year follow-up. At the beginning of the study, the average age was 10.2 ± 1.6 years, with 46.4% males and 90.7% ethnic Chinese. Children with high myopia (HM) were older and showed greater ODT (92% vs. 80%) and more PPA (94% vs. 73%) compared to those with low myopia (LM). RNFL thickness decreased in the superior, inferior, and nasal quadrants but increased in the temporal quadrant as myopia worsened. In the follow-up group, myopia progression was linked to thicker temporal quadrants and average RNFL, particularly in younger children. Previous treatment with myopia control lenses was also associated with increased RNFL thickness in the superior quadrant (Table 1).

Table 1. Multivariate Analysis of Factors Associated with RNFL

RNFL, µm	Optic Disc Tilt					Treatment				
	Grade 0	Grade 1		Grade 2		No Treatment	Atropine		Optical +/- Atropine	
	-	Coeff	P-value	Coeff	P-value	-	Coeff	P-value	Coeff	P-value
Average	ref	0.46	0.622	1.05	0.577	ref	0.57	0.519	2.32	0.072
Superior	ref	−0.19	0.906	−5.43	0.099	ref	−0.44	0.772	4.57	0.043
Inferior	ref	−0.14	0.932	−2.52	0.466	ref	0.32	0.841	1.78	0.452
Temporal	ref	9.86	<0.001	33	<0.001	ref	2.8	0.093	−0.22	0.927
Nasal	ref	−7.38	<0.001	−19.73	<0.001	ref	0.45	0.714	0.53	0.765

DISCUSSION

This study was conducted within a clinical cohort where many children were undergoing myopia treatment and its potential impact on RNFL thickness was considered. Notably, the study found that children treated with myopia control lenses exhibited increased RNFL thickness in the

superior region of the optic nerve head compared to those treated with topical atropine or those who received no treatment for myopia. Some studies have pointed out asymmetry in peripheral refraction in myopic eyes, with differing effects on the horizontal and vertical planes.[4] The superior retina seems to be especially susceptible to myopic changes.[5] The findings of this study suggest that myopia control glasses may impact ocular physiology in a way that differs from atropine treatment for myopia.

CONCLUSION

Children with higher myopia exhibit thinner RNFL in the nasal quadrant and thicker RNFL in the temporal quadrant around the optic nerve head, which is linked to ODT, even after adjusting for ocular magnification, compared to those with low myopia. Over two years, progressive myopia was associated with thicker average RNFL and RNFL in the temporal quadrant, suggesting distinct structural changes in the macular and non-macular areas of the eye in children. Myopia control lenses seemed to increase RNFL thickness specifically in the superior quadrant, when compared to atropine treatment or no treatment.

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Case report on Coats disease occurring with vitreous hemorrhage and neovascular glaucoma

INTRODUCTION

Coats disease is a vascular condition marked by retinal telangiectasia and aneurysms accompanied by exudation. The leaking blood vessels result in intraretinal and subretinal fluid accumulation, leading to outer retinal thickening. This may eventually cause partial or complete retinal detachment without retinal traction. If not treated, Coats disease can result in blindness and may require enucleation. Therefore, prompt diagnosis and treatment of Coats disease is essential for

preserving vision.[1] Coats disease typically affects one eye in young males during their first two decades of life, with an incidence rate of 0.09 per 100,000.[2] Common signs and symptoms of Coats disease include reduced visual acuity, strabismus, leukocoria, and pain. While most patients have a normal anterior segment, a small number may present with neovascular glaucoma (NVG), corneal edema, iris neovascularization, and megalocornea. The diagnosis is primarily made through clinical examination with indirect ophthalmoscopy, but fluorescein angiography (FA), optical coherence tomography (OCT), and ultrasound are also valuable diagnostic tools. On FA, areas of non-perfusion, early hyperfluorescence of telangiectasia that persists into the late stages, and hyperfluorescent exudation can help identify Coats disease. Telangiectasias and aneurysms appear as "light bulb" dilations due to the bulbous shape of the vessels and the surrounding yellow exudate.[1] This report describes an unusual case of Coats disease featuring NVG and vitreous hemorrhage.

Following vitrectomy, tube-shunt implantation, and several laser photocoagulation procedures guided by FA, patient in Coats disease showed a good visual prognosis.

CASE PRESENTATION

A 15-year-old Hispanic male presented with a five-day history of progressively worsening right eye pain, redness, and blurred vision upon waking. This was his first occurrence of such symptoms. On examination, the right eye revealed an intraocular pressure (IOP) of 53 mmHg, visual acuity of count fingers at 3 inches, a mid-dilated but reactive pupil, conjunctival injection, diffuse microcystic corneal edema, layered hyphema, and iris neovascularization at the pupillary margin. Gonioscopy showed peripheral anterior synechia in all quadrants. A posterior segment exam was hindered by anterior findings. Ultrasound revealed vitreous opacities and an inferior retinal detachment, but no obvious retinal tears, masses, or calcifications. Based on these findings, the patient was diagnosed with NVG and started on treatment aimed at lowering the elevated IOP and resolving corneal edema to improve visualization of the posterior segment. The treatment included topical carbonic anhydrase inhibitor and beta-blocker (dorzolamide/timolol) twice

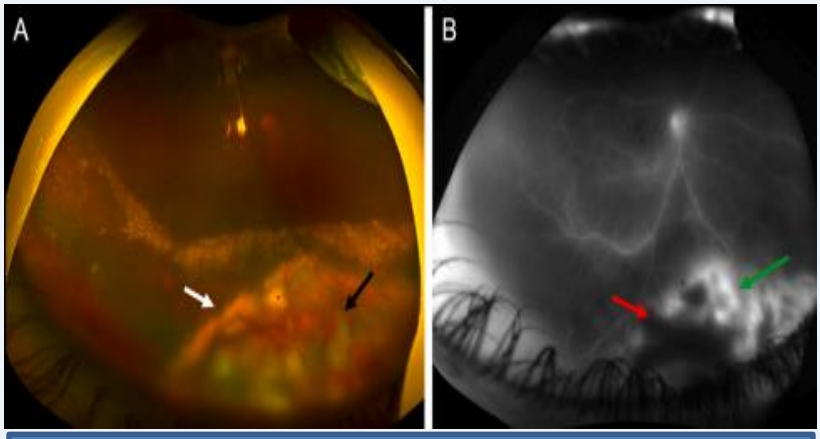

Figure 1. (A) An ultra-widefield fundus image showing telangiectatic vessels (black arrow) and exudative retinal detachment (white arrow) on the inferior side. (B) Late-phase fluorescein angiography showing arterial leakage (green arrow), "light bulb" dilations, and nonperfusion (red arrow).

daily, systemic acetazolamide, topical steroid (prednisolone acetate 1%) six times daily, and cyclopentolate 1% twice daily. Within a week, the patient's visual acuity improved to 20/100, IOP decreased to 30 mmHg, and symptoms subsided. The resolution of hyphema and decreased corneal edema allowed for better examination of the posterior segment, revealing vitreous hemorrhage and an exudative retinal detachment, extending inferotemporally and inferonasally while sparing the macula. FA showed diffuse vascular leakage along telangiectatic vessels, with "light bulb" dilations, indicative of Coats disease (Figure 1). With a negative workup, the diagnosis of Coats disease was confirmed. Due to persistent elevated IOP, netarsudil 0.02% was added to the regimen. Two weeks later, visual acuity improved to 20/60, although IOP remained elevated above 25 mmHg, likely due to the peripheral anterior synechia. Laser photocoagulation was performed on the exudative areas and telangiectatic vessels inferiorly, and intravitreal injection of bevacizumab was given due to NVG. Despite these treatments, elevated IOP and vitreous hemorrhage persisted, leading to a tube-shunt insertion and pars plana vitrectomy with endolaser. The procedure showed good laser uptake on the aneurysms and telangiectatic vessels. By postoperative day 4, IOP had improved to 10 mmHg, subretinal fluid had decreased, and the vitreous hemorrhage had clumped inferiorly. Prednisolone was tapered, and the patient was placed on only topical dorzolamide/timolol. Post-operative imaging revealed the progress, and three months later, FA showed persistent vascular leakage despite clinical improvement, leading to additional laser photocoagulation under general anesthesia. The exudative retinal detachment resolved, and over the following 18 months, the patient's best corrected visual acuity improved to 20/40, with IOP maintained below 12 mmHg. Follow-up FAs showed no vascular leakage, and management continued with topical dorzolamide/timolol. Imaging was taken after the final laser treatment but before the resolution of the exudative retinal detachment was documented.

DISCUSSION

This study reports a case of Coats disease presenting with an unusual combination of neovascular glaucoma and vitreous hemorrhage. Vitreous hemorrhage is an uncommon complication of Coats disease, as aneurysms in this condition typically do not rupture and are more often linked to exudative retinal detachment.[3] Although fluorescein angiography reveals capillary nonperfusion around the telangiectatic vessels, neovascularization is seldom seen, which likely accounts for the infrequent occurrence of vitreous hemorrhage in these eyes. Instead, vitreous hemorrhage may occur because of neovascularization secondary to long-standing retinal detachments.[4]

CONCLUSION

NVG is linked to a poor prognosis, and vitreous hemorrhage is an uncommon occurrence in Coats disease. Despite these challenges, the patient achieved a favorable visual outcome following vitrectomy, tube-shunt surgery, and multiple laser photocoagulation treatments guided by FA. Although the visual result was positive in this case, the underlying causes of Coats disease and its diverse presentations remain poorly understood.

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